Association of Retinal Vessel Caliber and Visual Field Defects in Glaucoma

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• PURPOSE: **This study evaluates the asymmetry of peripapillary retinal vessel caliber between inferior and superior hemispheres in eyes with visual field defects predominantly in one hemifield.**

• DESIGN: **Observational case series.**

• METHODS: **In a retrospective study, 64 eyes of 64 patients with primary open-angle glaucoma who had a marked difference in visual field defects between hemifields and who had no history of diabetes, trauma, or vascular occlusive disease were studied. The diameters of the superior and inferotemporal vessels were measured at the optic disk border with calipers on an enlarged image.**

• RESULTS: **In 64 eyes, the average ratio of the superior temporal artery diameter to inferotemporal artery diameter was significantly greater in the eyes with predominantly superior visual field defects as compared with those with inferior defects (1.10 ± 0.22 vs. 0.92 ± 0.19, respectively, $P = .002$, two-tailed *t* test). This indicates that the arteriole corresponding to the hemifield with the greater visual field defect was narrower than the arteriole in the other hemifield. This relationship was confirmed using χ^2 analysis ($P = .002$) comparing the proportions of eyes with ratios greater or less than normal vessel caliber ratios (normal ratio = 0.95 from data reported by Jonas and associates to the location of the dominant field defect. No statistically significant relationship was detected between retinal vein diameter and localized visual field defects, as determined by both the unpaired *t* test and χ^2 analysis.**

• CONCLUSION: **In eyes with primary open-angle glaucoma, this study demonstrates a strong association between decreased peripapillary arteriole diameter and visual field defects in the corresponding hemifield. This reflects either an ischemic basis for glaucomatous damage or vascular constriction when there are fewer axons to nourish.** **(Am J Ophthalmol 2001;132:855–859.**

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THE STUDY OF VASCULAR PATHOLOGY IN PRIMARY open-angle glaucoma is an active area of research. Several studies have looked at the connection between vessel caliber and glaucoma. Jonas and associates[1] studied the caliber of retinal vessels adjacent to the optic disk in patients with glaucoma and those without glaucoma by measuring the superotemporal and inferotemporal retinal arteries and veins. They found that the peripapillary retinal vessel diameters (both arteries and veins) were significantly smaller in eyes with glaucoma than controls. They used their data to establish normal values for the caliber of the retinal vessels. Other studies have demonstrated focal narrowing of retinal vessels adjacent to the disk in glaucomatous eyes, and correlated this to morphologic changes of the optic nerve, peripapillary retina, and nerve fiber layer. Rankin and associates[2] reported a correlation between focal arteriolar narrowing and visual field defects in the corresponding hemifield. However, this observation was not the main focus of their study, and accordingly, subjects were not selected on the basis of localized visual field defects.

In the current study, we measured the peripapillary blood vessels in eyes with open-angle glaucoma and visual field defects localized predominantly to the superior or inferior hemifield. We used the ratio of superotemporal to inferotemporal vessel diameter to correlate relative vessel diameters to the location of perimetric defects. In addition, we used the normative values measured by Jonas and associates,[1] to evaluate the relationship between vessel diameters and localized visual field defects. We hypothesized that subjects with predominantly superior visual field defects would have narrowing of the inferior vessels and those with predominantly inferior defects would have narrowing of the superior vessels. The ratio of the diameter of the superior vessel to inferior vessel would therefore be greater than normal in subjects with predominantly superior visual field defects and less than normal in subjects with inferior field defects (Table 1).

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TABLE 1. Study Hypothesis*

Visual Field Defect	Vessel Narrowing	Ratio: Superior Vessel Diameter/Inferior Vessel Diameter
Superior hemifield	Inferior vessel	>Normal
Inferior hemifield	Superior vessel	<Normal

*It was hypothesized that subjects with predominantly superior visual field defects would have narrowing of the inferior vessels and those with predominantly inferior defects would have narrowing of the superior vessels. The ratio of the diameter of the superior vessel to inferior vessel would therefore be greater than normal in subjects with predominantly superior visual field defects and less than normal for subjects with inferior field defects.

METHODS

A SEARCH OF MORE THAN 4000 CHARTS NETTED 64 THAT satisfied the inclusion criteria for this study. Inclusion criteria consisted of a diagnosis of primary open-angle glaucoma, fundus photographs taken within one year of corresponding visual fields tests and the presence of asymmetric visual fields. Exclusion criteria included a history of diabetes, trauma, or vascular occlusive disease.

Asymmetric Goldmann visual fields were defined as having either an arcuate or nasal step scotoma of at least 20 degrees to the III4e isopter in the more involved hemifield; the less involved hemifield had no more than a 10 degree arcuate scotoma to the I4e isopter and no nasal step defect. Threshold automated visual fields (Octopus program 32 or G1) required a minimum of five contiguous nonedge points with thresholds decreased by at least 10 decibels from age matched controls in the more affected hemifield, while the other hemifield had no more than one nonedge point similarly depressed. Only one eye/subject was included in the study. In cases in which both eyes had asymmetric visual field defects satisfying these criteria, the eye with the greater disparity between hemifields was used. Also, in the case of both manual and automated visual fields within 1 year of the fundus photographs, the automated field was used preferentially. All fundus photographs had to be of superior quality with meticulous focusing of the retinal vessels.

A total of 64 1X color fundus photographs of 64 eyes were used. All measurements were performed within a 2-week interval by the same observer. The observer was masked to the visual field defect corresponding to the fundus photographs and was further masked to the optic disk cupping by an opaque tape covering all but the edge of the disk (Figure 1). The observer used the same standard system of calipers on a magnified image for each measurement, making all measurements at the optic disk border. As several studies evaluating the reproducibility of measurements found repeated measurements more reliable,[3] five measurements were performed for each vessel and were averaged. To evaluate the reproducibility of our measurements, five of the eyes were randomly remeasured five times. The observer was unaware of which slides were used to measure reproducibility.

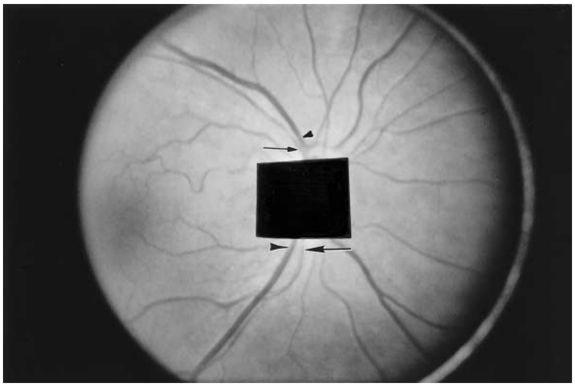

FIGURE 1. Fundus photograph illustrating masking of optic disk cupping. Note: superior temporal arteriole (small arrow); inferior temporal arteriole (large arrow); superior temporal vein (small arrowhead); inferior temporal vein (large arrowhead).

TABLE 2. Location of Visual Field Defect Versus the Ratio of Superior Temporal Artery/Inferior Temporal Artery Calibers

Visual Field Defect	*n*	Mean Ratio*	Standard Deviation
Superior hemifield	42	1.10	0.215
Inferior hemifield	22	0.92	0.188

*$P = 0.002$; Comparison between mean ratio of superior temporal artery/inferior temporal artery caliber in eyes with superior hemifield visual field defects versus inferior hemifield visual field defects (unpaired two-tailed *t* test).

The ratio of the superotemporal artery to the inferotemporal artery and also the ratio of the superotemporal vein to the inferotemporal vein were calculated and statistical analysis of the data performed. Mean ratios for arterioles and veins from eyes with predominantly superior defects were compared with those for eyes with predominantly inferior defects using unpaired *t* tests (Tables 2 and 3).

A normal value for the ratio of superotemporal arteriole to inferotemporal arteriole and one for superotemporal vein to inferotemporal vein were calculated using data from Jonas and associates[1] These values were calculated to be 0.954 and 0.942, respectively. χ^2 analysis was performed to compare the number of eyes with ratios greater or less than the normal value in eyes with superior versus inferior field defects (Tables 4 and 5).

TABLE 3. Location of Visual Field Defect Versus the Ratio of Superior Temporal Vein/Inferior Temporal Vein Calibers

Visual Field Defect	*n*	Mean Ratio*	Standard Deviation
Superior hemifield	42	1.01	0.209
Inferior hemifield	22	0.96	0.188

*P = 0.345; Comparison between mean ratio of superior temporal vein/inferior temporal vein caliber in eyes with superior hemifield visual field defects versus inferior hemifield visual field defects (unpaired two-tailed t test).

TABLE 4. Location of Visual Field Defect Versus Number of Eyes with Superior Temporal Artery/Inferior Temporal Artery Ratio Less Than and Greater Than Normal Ratio*

	STA/ITA <Normal (<0.954)	STA/ITA >Normal (>0.954)	Total
Superior hemifield defect	9	33	42
Inferior hemifield defect	14	8	22
Total	23	41	64

*P = 0.002 (chi-square analysis).
STA = Superior temporal artery; ITA = Inferior temporal artery.

RESULTS

THE AVERAGE PATIENT AGE WAS 65.8 YEARS OLD WITH AN age range of 31 to 87 years. The group included 26 males and 38 females. Twenty-three patients carried a diagnosis of systemic hypertension. Other common systemic diseases included thyroid abnormalities, asthma, and arthritis. Corrected visual acuity had a range from 6/5 to 6/18 with 45 eyes having visual acuity of 6/7.5 or better. The cup-to-disk ratio averaged 0.82 with a range of 0.6 to 0.95. All patients used topical therapy, alone or in combination, as follows: 41 patients were on nonselective topical beta blockers, five on betaxolol, 29 on pilocarpine, and 24 on an adrenergic agonist. Fourteen patients had undergone argon laser trabeculoplasty, while five had undergone surgical trabeculectomy. Of the eyes which qualified for this study, 34 were left eyes and 30 were right eyes.

Superior visual field defects outnumbered inferior visual field defects by 42 to 22. The method of visual field measurement was equally split between automated and manual fields: 32 each. The involved hemifield for automated fields had an average of 13 contiguous nonedge points depressed 10 decibels from age-matched controls.

Our results showed that the average ratio of superotemporal to inferotemporal peripapillary arteriole caliber was 1.10 ± 0.22 for eyes with predominantly superior visual field defects and 0.92 ± 0.19 for eyes with predominantly inferior visual field defects. This difference between the mean ratios was statistically significant (P = .002, two tailed t test), and indicates that the arteriole corresponding to the hemifield with the greater visual field defect was narrower than the arteriole in the other hemifield (Tables 1 and 2).

This relationship was confirmed using χ^2 analysis (Table 4). From the normative data by Jonas and associates,[1] an average ratio of the superotemporal artery to the inferotemporal artery for normals was calculated to be 0.954. The proportion of eyes with ratios greater or less than this value was compared with the location of the dominant field defect. Significantly more eyes with predominantly superior visual field defects had ratios greater than normal, indicating narrowing of the inferior peripapillary arteriole. Significantly more eyes with predominantly inferior visual field defects had ratios less than normal, indicating narrowing of the superior peripapillary arteriole. This analysis supports the original hypothesis.

No statistically significant association was detected between retinal vein diameter and localized visual field defects. The ratio of the superotemporal vein to the inferotemporal vein was not significantly different in eyes with superior visual field defects compared with inferior visual field defects (Table 3). Also, χ^2 analysis of the ratio of the superotemporal to inferotemporal vein, using normative data derived from Jonas and associates,[1] showed no statistically significant relationship (Table 5).

The results of the reproducibility measurements showed a high degree of reproducibility of the measurements, with two standard deviations of approximately 0.05 (Table 6).

TABLE 5. Location of Visual Field Defect Versus Number of Eyes With Superior Temporal Vein/Inferior Temporal Vein Ratio Less Than and Greater Than Normal Ratio*

	STA/ITV <Normal (<0.942)	STA/ITV >Normal (>0.942)	Total
Superior hemifield defect	16	26	42
Inferior hemifield defect	9	13	22
Total	25	39	64

*P = 0.960 (chi-square analysis).
STV = Superior temporal vein; ITV = Inferior temporal vein.

DISCUSSION

THIS STUDY DEMONSTRATES A STRONG ASSOCIATION BETWEEN retinal arteriole diameter and localized visual field defects in primary open angle glaucoma. We correlated visual field loss predominantly in one hemifield with peripapillary vessel narrowing in the corresponding hemisphere of the retina. We used strict criteria to select eyes with distinct hemifield visual field loss.

TABLE 6. Reproducibility of Vessel Measurements

Slide	Mean	Standard Deviation	Standard Deviation as % of Mean
1	0.89	0.05	5.39
2	1.14	0.01	1.05
3	0.90	0.01	1.32
4	0.73	0.05	7.02
5	1.04	0.01	1.09

The ratio of the diameter of the superotemporal artery to the inferotemporal artery was used to define vessel narrowing, negating the need for absolute measurements. Use of this ratio provides a measure of relative constriction between the two hemifields. To obtain absolute measurements of structures from fundus photographs, formulas must be used which provide only an estimate of the true measurement and can potentially introduce significant inaccuracy into the measurement. The use of ratios allows detection of narrowing that might be missed via absolute measurement techniques. It also focuses attention on regional differences in vessel caliber within the retina.

Additionally, measuring relative constriction within one subject's eye provides an internal control, and thereby minimizes the effect of confounding factors which may influence vessel diameters in different individuals. Some significant confounding factors minimized via this method include medications, concurrent disease, and age of the subject. However, the use of the ratio does not allow us to evaluate vascular constriction that may be occurring in both hemifields. We are unable to determine if the relatively unaffected hemifield has normal or constricted vessels.

Previous studies have documented decreased retinal vessel caliber in glaucomatous eyes, and its association with morphologic changes.[1,2,4–7] This decrease has been correlated with increased peripapillary chorioretinal atrophy, decreased neuroretinal rim area, increased cup/disk ratios,[4,7] and decreased retinal nerve fiber layer.[4] Although the bulk of the correlations were morphologic, Jonas and associates[4] and Lee and associates[7] also found that narrowing of peripapillary retinal vessel diameter correlated with perimetric defects. Our findings support previous investigations.[2,7] However, our specific selection of subjects with asymmetric visual field loss located primarily in one hemifield, as well as our use of ratios of vessel diameter to compare measurements, distinguishes this study.

It has not yet been demonstrated definitively whether peripapillary vessel narrowing causes damage to the optic nerve or whether the reverse is true. Loss of retinal ganglion cells may cause a decrease in retinal vessel caliber via autoregulatory mechanisms responding to a decreased regional demand for oxygen.[1,5,6,8] This is supported by observations that vessel narrowing is not specific to glaucoma. Decreased vessel diameter is also found in nonglaucomatous optic neuropathies such as nonarteritic anterior ischemic optic neuropathy and descending optic nerve atrophy.[2,6] In addition, the degree of narrowing has been correlated with the degree of optic atrophy more closely than with the particular disease.[5,9] In contrast, diminished blood flow in the optic nerve has been detected early in the course of glaucoma which suggests this vascular impairment may precede glaucomatous optic neuropathy.[10]

It is worth considering the possible role of vasospasm in the observed narrowing of vessels in this study.[2] The possibility must be considered that our fundus photographs caught some vessels in the midst of a vasospasm. Though this may be a small confounding factor, several studies suggest that the location of arteriolar narrowing is constant over time.[2,6] Papastathopoulos and associates found no significant change in the location of vessel narrowing in their subjects over a period of at least 8 months.[6] In addition, these same investigators compared narrowed vessels seen on fundus photographs to the same vessels seen on fluorescein angiograms and found "significant correlation" of vessel diameter.[6] Rankin and associates investigated a possible relationship between systemic vasospasm and retinal vessel narrowing, but found no significant correlation between digital vasospasm in response to cold and retinal vessel narrowing.[2] However, they do report one case of reversible focal narrowing of peripapillary arterioles.[2]

It is unclear if topical medications predispose patients to narrowing of peripapillary vessels.[11–14] By using the ratio of vessel diameters within one subject's eye, this potentially confounding factor is minimized.

In eyes with primary open-angle glaucoma, this study demonstrates a strong association between decreased peripapillary arteriole diameter and visual field defects in the corresponding hemifield. The question remains as to whether this is a reflection of an ischemic basis for glaucomatous damage or a result of vascular constriction when there are fewer axons to nourish. Understanding the process leading to peripapillary vessel narrowing would further our understanding of the importance of this clinical finding.

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